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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/756,543	01/08/2001	Richard A. Young	0399.1185-006	6739
26161	7590	10/07/2003		
FISH & RICHARDSON PC 225 FRANKLIN ST BOSTON, MA 02110			EXAMINER BELYAVSKIY, MICHAEL A	
			ART UNIT	PAPER NUMBER

1644

DATE MAILED: 10/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/756,543	YOUNG, RICHARD A.	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 July 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-8 and 25-44 is/are pending in the application.
- 4a) Of the above claim(s) 7,25,26, 36,38 and 39 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 27-35, 37 and 40-44 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 07/31/03 is acknowledged.

Claims 1-8 and 25-44 are pending.

2. The amended claim 7 and newly submitted claims 25, 26, 36, 38 and 39 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: Originally elected species of heat shock protein and moiety in claims 1-24, now claims 1-5, 27-34, 37 and 40-44 drawn to a method of delivering a moiety of interest into a cells, comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a heat shock protein, wherein heat shock protein is a hsp70 mycobacterial heat shock protein and the moiety is a protein are under consideration in the instant application. Amended claims 6 and 7 and newly submitted claims 25, 26, 35, 36, 38 and 39 drawn to a method of delivering a moiety of interest into a cells, comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a heat shock protein, wherein heat shock protein is non-elected species as recited in claim 6 and 7, 26, 35, 36 and 39 and wherein the moiety of interest is non-elected species as recited in claims 25 and 38.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 6, 7, 25, 26, 35, 36, 38 and 39 withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-6, 8, 27-35, 37 and 40-44 drawn to a method of delivering a moiety of interest into a cells, comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a heat shock protein, wherein heat shock protein is a hsp70 mycobacterial heat shock protein and the moiety is a protein under consideration in the instant application.

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The following new ground of rejection are necessitated by the amendment filed 6/12/02(Paper No. 13).

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 31 and 44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 31 and 44 are indefinite and ambiguous in the recitation of “ wherein the portion of the hsp is a protein”. It is unclear what Applicant intended to claim because hsp is a heat shock protein itself. What else a portion of said protein can be ?

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-6, 8, 27-35, 37 and 40-44 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

A method of delivering a moiety of interest into a cells, comprising contacting the cell with a complex comprising the moiety of interest covalently linked to “a protein consisting of a portion of heat shock protein (hsp) “and “the portion of the hsp is sufficient to deliver the moiety into the cells”, claimed in Claim 1; “protein or peptide is glycosylated” , claimed in claims 8 and 37 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from. The specification and the claims as originally filed only support for a method of delivering a moiety of interest into a cells, comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a heat shock protein , wherein the moiety is a protein.

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7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1-6, 8, 27-35, 37 and 40-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over Suzue et al. (1996, Reference AZ3 in IDS) or over Barrios et al. (1992, Reference AU in IDS) both in view of Srivastava et al. (1994, Reference AV4 in IDS) and US Patent 6,403,099.

Suzue et al. teach a method of *in vivo* delivering a moiety of interest into an antigen presenting cell of an individual, comprising contacting a cell with a complex, comprising an HIV covalently linked to mycobacteria heat shock protein 70 (see entire document, Abstract in particular). Suzue et al. teach a fusion protein comprising mycobacterial hps70 – HIV-1 p24 (see Materials and Methods in particular, pages 873 to 875). Suzue et al. also teach that administration of this fusion protein to mice induces a strong immune response (see page 875, 1st column and page 876 2nd column in particular). Suzue et al. also teach that the coupling must be covalent in order to be maximally efficacious (see page 876, 2nd column in particular).

Barrios et al. teach the method of *in vivo* delivering a protein to an individual in such ways to induced an immune response using a protein covalently coupled to a mycobacterial hsp70 (see entire reference, Abstract in particular). Barrios et al. teach the making of a glutaraldehyde covalently crosslinked complex of mycobacterial hsp70 and proteins (see pages 1366 in particular). Barrios et al. teach that administration of this complex into mice induces a strong immune response and that the coupling must be covalent in order to be maximally efficacious (see page 1386 in particular). Barrios et al. teach that the effect observed may be due to increased cellular uptake of the antigen complex by antigen processing cells because of the chaperone function of the HSP70 (see page 1371 in particular).

Suzue et al., or Barrios et al., do not explicitly teach that HSP's with antigens are processed by uptake into macrophages or other antigen presenting cells and that moiety of interest covalently linked to a portion of a heat shock protein.

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The mechanism that the complexes of HSP's with antigens are processed by uptake into macrophages or other antigen presenting cells with re-expression of antigenic peptides on the surface of the antigen presenting cells for presentation to T cells (in particular Srivastava et al., page 729, 2nd column, lines 20-22 , 25-30 and page 730, 1st column , lines 7-11 and 19) is obvious in the structure of the hsp-antigen conjugate and the general properties of the immune response. If an antigen is immunogenic then it is taken up by cells as per immediately above encompassing claims 1, 5 and 40 . It was known at the time the invention was made that the immunogenicity of a heat shock protein-antigen complex was a function of the uptake of the complex by antigen presenting cells (see Srivastava et al. above) thus encompassing claims 5 and 40.

US Patent '099 teaches a conjugate compound comprising a heat shock protein or portion thereof covalently linked to a moiety of interest to induced an immune response in individual, including human. (see entire document, Abstract in particular). US Patent '099 teaches that heat shock protein or portion of said protein is mycobacterial hsp 70 (see column 2, lines 31-55 in particular) . Patent '099 teaches that skilled in the art can prepare modified heat shock protein containing only portions of a heat shock protein that are sufficient to deliver the moiety into the cell (see column 3, lines 15-25 in particular).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of US Patent '099 to those of Suzue et al., or Barrios et al to obtain a claimed method of delivering a moiety of interest into a cell, the method comprising contacting the cell with a complex comprising the moiety of interest covalently linked to a portion of a heat shock protein.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because that skilled in the art can prepare modified heat shock protein containing only portions of a heat shock protein that are sufficient to deliver the moiety into the cell as taught by US Patent '099. Said complex, comprising a portion of a heat shock protein and moiety of interest can substitute the complex comprising full length heat shock protein and moiety of interest as taught by Suzue et al., or Barrios et al in a method of delivering a moiety of interest into a cell.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 6 and 35 are included because a generic term " bacterial heat shock protein" would include mycobacteria heat shock protein 70.

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Claims 31 and 41 are included because it was well known in the art at the time the invention was made that N-terminal amino acid of hsp70 constitutes a ATP binding domain of a molecule and that the ATP binding function of hsp70 is involved in the efficient transfer of antigenic peptides into the MHC class I antigen presentation pathway.

9. No claim allowed

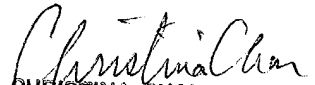
10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
October 6, 2003


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